BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Thomas B. Knudsen	Developmental Systems Biologist (title 42) National Center for Computational Toxicology
eRA COMMONS USER NAME T0KNUD01	

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Albright College, Reading PA	B.S.	1976	Biology
Thomas Jefferson University, Philadelphia PA	Ph.D.	1981	Anatomy
Children's Hospital, Cincinnati OH	Postdoc	1981-82	Cell Biology
Emory University, Atlanta GA	Postdoc	1982-86	Developmental Biology

A. POSITIONS and HONORS

Research and Professional Experience:

1986-90 Assistant Professor, Dept. of Anatomy, E. Tenn. State University, Johnson City TN
1990-03 Asst./Assc./Full Prof. (tenured) Path. Anat. Cell Biol., Thomas Jefferson University, Philadelphia PA
2003-pres. Editor-in-Chief, *Reproductive Toxicology* (Elsevier)
2004-07 Professor (tenured), Mol. Cell & Craniofacial Biol., U of Louisville, School of Dentistry, Louisville KY
2004-07 Director, Systems Analysis Laboratory, U of Louisville, Birth Defects Center
2004-pres. Member, Center for Genetics and Molecular Medicine, U Louisville, Louisville KY
2005-07 Professor of Biochemistry and Molecular Biology (joint appointment), U Louisville
2007-pres. Center for Environ. Genomics & Integrative Biol., U Louisville
2007-pres. Clinical and Translational Science Institute, Louisville, Biomedical Informatics Group
2007-pres. Professor Molecular, Cellular & Craniof. Biol., U of Louisville, School of Dentistry, Louisville KY
2007-pres. Developmental Systems Biologist (title 42), NCCT, US Environmental Protection Agency, RTP NC

Professional Societies and Affiliations:

American Association for the Advancement of Science (AAAS), American Society of Cell Biology (ASCB), Federation of American Societies for Experimental Biology (FASEB), Sigma Xi, Teratology Society, Society of Toxicology, European Teratology Society

Honors and Awards:

Fellowships: NIH Predoctoral trainee, T32 HD07075 (1977-80)
NIH Postdoctoral trainee, F32 HD06212 (1982-85)

Federal grants (PI): NIH/NICHD grant R29 HD24143 (1989-94)
NIH/NICHD grant RO1 HD30302 (1993-98)
US EPA grant CR 824445 (1995-99)
NIH/NIEHS grant RO1 ES09120 (1998-01)
NIH/NIEHS grant 1 R13 ES012410 (2003)
US EPA-NCERQA grant R 827445-01-0 (1999-03)
NIH/NIAAA grant RO1AA13205 (2001-08)
NIH/NIEHS grant 1 R13 ES013116 (2004)
NIH/NIEHS grant 2 RO1 ES09120 (2001-07)
NIH/NIEHS Training grant T32 ES07282 (1998-08)
NIH/NIEHS grant 1 R21 ES013821-01 (2005-08)

Special Recognition: NIH Human Embryology & Development II Study Section, (1994-98); FASEB delegate, (1998-01); Councilor, Teratology Society (1999-02); Wilson Publication Award, Teratology Society (2002); Chair, Bioinformatics Committee, Teratology Society (2002-05); University Scholar, U Louisville (2003-08); Research!Louisville: 3rd place, Innovation in Biotechnology (2004); President - Teratology Society (2007-08).

Selected Invitations at National & International Symposia (last 3 years):
Systems Biology: a new venue for exploring mechanisms of developmental toxicity (SOT 2004), *Chair*
Web-based resources for Teaching Human Embryology (FASEB-AAA, Washington DC 2004), *Speaker*
Birth Defects Systems Manager and Teratology Analyzer (Teratology Soc. Vancouver BC 2004), *Speaker*
Experimental Design & Interpretation of Gene Arrays in Dev Biol-Tox (ETS Thessaloniki, 2004), *Speaker*
Computational Systems Analysis of Devel. Tox. Using Microarray Data (Toxicogenom. Kyoto 2004), *Speaker*
Computational Systems Analysis of a Disease Network (Neuroprotective Agents. Asilomar 2004), *Speaker*
PBR in Embryo Development (Working group for renaming the PBR, Washington D.C. 2004), *Speaker*
Computational Systems Analysis of Developmental Toxicity (SOT, New Orleans 2005), *Speaker*
Synthesis of Exp and Comput. Approaches in Develop Tox. (Henry Stewart Conf 2005), *Speaker*
Database resource for birth defects and developmental toxicity (Teratol. Soc. St. Petersburg, 2005), *Speaker*
Computational systems analysis of developmental toxicology (ETS Haarlem, 2005), *Speaker*
Genes for low-dose reg. of the embryonic transcriptome (Hormesis - 6th Int Conf, Amherst 2007), *Speaker*
Computational Toxicology: New Approaches to Improve Env. Hlth Prot. (RIVM, Bilthoven NL 2007), *Speaker*
Genomics as a tool in developmental toxicology (Eurotox, Amsterdam 2007), *Speaker*
Computational Toxicology: New Approaches to Improve Env. Hlth Prot. (AIHA-SOT, Louisville 2007), *Speaker*
Computational Framework to Predict Toxicity & Prioritize Testing of Env. Chem. (NCAC-SOT 2007), *Speaker*

B. SELECTED PUBLICATIONS (selected from ~65 total).

Chinsky JM, Ramamurthy V, Fanslow WC, Ingolia DE, Blackburn MR, Shaffer KT, Higley HR, Trentin JJ, Rudolph FB, **Knudsen TB**, and Kellems RE (1990) Developmental expression of adenosine deaminase in the upper alimentary tract of mice Differentiation 42: 172-183.

Airhart MJ, Roberts MA, **Knudsen TB** and Skalko, RG (1990) Axonal guidance of adenosine deaminase immunoreactive primary afferent fibers in developing mouse spinal cord Brain Res Bull 25: 299-309.

Hong L, Mulholland J, Chinsky JM, **Knudsen TB**, Kellems RE and Glasser SR (1991) developmental expression of adenosine deaminase during decidualization in the rat uterus Biol Reprod 43: 83-93.

Knudsen TB, Blackburn MR, Chinsky JM, Airhart MJ and Kellems RE (1991) Ontogeny of adenosine deaminase in the mouse decidua and placenta: immunolocalization and embryo transfer studies. Biol. Reprod. 43: 171-184.

Knudsen TB, Winters RS, Otey SK, Blackburn MR, Airhart MJ, Church JK and Skalko RG (1992) Effects of (R)-deoxycoformycin (pentostatin) on intrauterine nucleoside catabolism and embryo viability in the pregnant mouse. Teratology 45: 91-103.

Blackburn MR, Gao X, Airhart MJ, Skalko RG, Thompson LF and **Knudsen TB** (1992) Adenosine levels in the early postimplantation mouse uterus. Quantitative analysis by HPLC-fluorometric detection and spatio-temporal regulation by 5'-nucleotidase and adenosine deaminase. Dev. Dynam. 194: 155-168.

Gao X, Blackburn MR and **Knudsen TB** (1994) Activation of apoptosis in early mouse embryos by 2'-deoxyadenosine exposure. Teratology 48: 1-12.

Gao X, **Knudsen TB**, Ibrahim MM and Haldar S (1995) Bcl-2 relieves deoxyadenylate stress and suppresses apoptosis in Pre-B leukemia cells. Cell Death Different. 2: 69-78.

Puffinbarger NK, Hansen KR, Resta R, Laurent AB, **Knudsen TB**, Madara JL and Thompson LF (1995) Production and characterization of multiple antigenic peptide antibodies to the adenosine A2b receptor. Mol Pharmacol 47: 1126-1132.

Ibrahim MM, Weber IT and **Knudsen TB** (1995) Mutagenesis of human adenosine deaminase to active forms that partially resist inhibition by pentostatin. Biochem. Biophys. Res. Commn. 209: 407-416.

Wubah JA, Ibrahim MM, Gao X, Nguyen D, Pisano MM and **Knudsen TB** (1996) Teratogen-induced eye defects mediated by p53-dependent apoptosis. Current Biology 6:60-69.

Resta R, Hooker SW, Laurent AB, Rahman SMJ, Franklin M, **Knudsen TB**, Nadon NL and Thompson LF (1997) Insights into thymic purine metabolism and adenosine deaminase deficiency revealed by transgenic mice overexpressing ecto-5'-nucleotidase (CD73). J Clin Invest 99: 676-683.

Blackburn MR, **Knudsen TB** and Kellems RE (1997) Genetically engineered mice demonstrate that adenosine deaminase is essential for early postimplantation development. Development 124: 3089-97

Knudsen TB (1997) Genetic and Cellular Pathways in Teratogen-Induced Cell Death. In *Comprehensive Toxicology* (Vol. 10), Sipes IG, McQueen CA and Gandolfi AJ (eds.), New York: Pergamon, pp. 529-534.

Knudsen TB and Wubah JA (1998) Transgenic animal models. Functional analysis of developmental toxicity as illustrated with the p53 suppressor model. In *Handbook of Developmental Neurotoxicology*, Slikker, W. Jr. and Chang, L.W. (eds.), San Diego: Academic Press, pp 209-221.

Ibrahim MM, Razmara M, Nguyen D, Donahue RJ, Wubah JA and **Knudsen TB** (1998) Altered expression of mitochondrial 16S ribosomal RNA in p53-deficient mouse embryos revealed by differential display. Biochem Biophys Acta 1403: 254-264.

Blackburn MR, Wubah JA, Thompson LF and **Knudsen TB** (1999) Transitory expression of the A2b adenosine receptor during implantation chamber development. Devel Dynam 216: 127-136.

Knudsen TB (1999) HPLC-based mRNA differential display. In: *Developmental Biology Protocols* (vol. II), Tuan, R.S. and Lo, C.W. (eds.). Totowa: Humana Press, Inc., pp 337-341.

Knudsen TB (2000) Mitochondrial transduction of teratogenesis. Teratology 62: 238-239.

Donahue RJ, Razmara M, Hoek JB and **Knudsen TB** (2001) Direct influence of the p53 tumor suppressor on mitochondrial biogenesis and function. FASEB J 15: 635-644.

Wubah JA, Setzer RW, Lau C, Charlap JH and **Knudsen TB** (2001) Exposure-disease continuum for 2-chloro-2'-deoxyadenosine, a prototype ocular teratogen. I. Dose-response analysis. Teratology 64: 154-169.

O'Hara MF, Charlap JH, Craig RC and **Knudsen TB** (2002) Mitochondrial transduction of ocular teratogenesis during methylmercury exposure. Teratology 65:131-144.

Lau C, Narotsky MG, Lui D, Best D, Setzer RW, Mann PC, Wubah JA and **Knudsen TB** (2002) Exposure-disease continuum for 2-chloro-2'-deoxyadenosine, a prototype teratogen. II. Induction of lumbar hernia in the rat and species comparison for the teratogenic responses. Teratology 66: 6-18.

Knudsen TB, Charlap JH and Nemeth KA (2003) Microarray applications in developmental toxicology. In: *Perspectives in Gene Expression.* K. Appasani, ed. Eaton Publishing/BioTechniques Press, Westboro MA. pp 173-194.

Charlap JC, Donahue RJ and **Knudsen TB** (2003) Exposure-disease continuum for 2-chloro-2'-deoxyadenosine, a prototype ocular teratogen. 3. Intervention with PK11195. Birth Defects Res (A) 67: 108-115.

O'Hara MF, Nibbio BJ, Craig RC, Nemeth KR, Charlap JH and **Knudsen TB** (2003) Mitochondrial benzodiazepine receptors regulate oxygen homeostasis in the early mouse embryo. Repro Tox 17: 365-375.

Lee JW, Park J, Jang B and **Knudsen TB** (2004) Altered Expression of Genes Related to Zinc Homeostasis in Early mouse Embryos Exposed to Di-2-ethylhexyl phthalate. Toxicol Lett 152: 1-10.

Knudsen TB and Green ML (2004) Response characteristics of the mitochondrial DNA genome in developmental health and disease. Birth Defects Res (C) 72: 313-329.

Singh AV, Knudsen KB and **Knudsen TB** (2005) Computational systems analysis of developmental toxicity: design, development and implementation of a birth defects systems manager (BDSM). Reprod Tox 19: 421-439.

Knudsen TB (2005) How can we use bioinformatics to predict which agents will cause birth defects? In: Primer in Teratology (B Hales and A Scialli, eds) Teratology Society Chapter 20, pp- 58-59

Szabo G, Hoek JB, Darley-Usmar V, Hajnoczky G, **Knudsen TB**, Mochly-Rosen D, and Zakhari, S (2005) RSA 2004: Combined basic research satellite symposium – session three: Alcohol and Mitochondrial Metabolism: AT the crossroads of life and death. Alcoh. Clin. Exp. Res. 29: 1749-1752.

Nemeth KA, Singh AV and **Knudsen TB** (2005) Searching for biomarkers of developmental toxicity with microarrays: normal eye morphogenesis in rodent embryos. Toxicol Appl Pharmacol. 206: 219-228.

Knudsen KB, Singh AV and **Knudsen TB** (2005) Data input module for Birth Defects Systems Manager. Reprod Tox 20: 369-375.

Slikker W Jr, Young JF, Corley RA, Dorman DC, Conolly RB, **Knudsen TB,** Erstad BL, Luecke RH, Faustman EM, Timchalk C and Mattison DR (2005) Improving predictive modeling in pediatric drug development: pharmacokinetics, pharmacodynamics and mechanistic modeling. Ann NY Acad Sci 1053: 505-518.

Kinane DF, Shiba H, Stathopoulou PG, Zhao H, Lappin DF, Singh AV, Eskan MA, Beckers S, Weigel S, Alpert B and **Knudsen TB** (2006) Gingival epithelial cells heterozygous for Toll-like receptor 4 polymorphisms Asp299Gly and Thr399Ile are hypo-responsive to Porphyromonas gingivalis. Genes & Immun 7: 190-200.

Papadopoulos V, Baraldi M, TR Guilarte, **Knudsen TB**, Lacapère JJ, Lindemann P, Norenberg MD, Nutt D, Poupon MF, Weizman A, Zhang MR and Gavish M. (2006) TspO: New Nomenclature for the peripheral-type Benzodiazepine receptor / recognition Site (PBR) based on its structure and molecular function. Trends in Pharmacol Sci. 8: 402-409.

Green ML, Singh AV, Zhang Y, Nemeth KA, Sulik KK and **Knudsen TB** (2007) Reprogramming of genetic networks during initiation of the fetal alcohol syndrome. Devel Dynam 236: 613-631.

Singh AV, Knudsen KB and **Knudsen TB** (2007) Integrative Analysis of the mouse embryonic transcriptome. Bioinformation 1: 24-30.

Singh AV, Rouhka EC, Rempala GA, Bastian CD and **Knudsen TB** (2007) Integrative database management for mouse development: systems and concepts. Birth Defects Res (C): 81: 1-19.

Calabrese EJ, et al., **Knudsen TB**, et al. (2007) Biological Stress Response Terminology: Integrating the concepts of adaptive response and preconditioning stress within a hormetic dose-response framework Toxicol Appl Pharmacol (*in press*)

Deaciuc IV, Song Z, Peng X, Barve SS, Song M, He Q, **Knudsen TB**, Singh AV, and McClain CJ (2007) Genome-wide transcriptome expression in the liver of a mouse model of high carbohydrate diet-induced liver steatosis and its significance for the disease. Hepatol International (*in press*)

Barthold JS, McCahan, Singh AV, **Knudsen TB**, Si X, Campion L and Akins RE (2007) Altered expression of muscle and cytoskeleton-related genes in a rat strain with inherited cryptorchidism. J Androl. (*revised manuscript under review*).

Datta S, Turner D, Singh R, Ruest LB, Pierce WM Jr and **Knudsen TB** (2007) Fetal Alcohol Syndrome (FAS) in C57BL/6 mice detected through proteomics screening of the amniotic fluid Birth Defects Res (Part A) (*revised manuscript under review*)

Johnson CS, Sulik KK, Wood C, Schmid JE, **Knudsen TB** and Hunter ES III (2007) A microarray analysis exploring ethanol's teratogenesis in the mouse forelimb. Reprod Tox (*under revision*)

C. RESEARCH SUPPORT (Completed, last 3 years)

NIH 2 R56-AA13205-05 Knudsen (PI) 09/29/01 – 05/31/08
Response Signatures of Alcohol Related Birth Defects

NIH R21-ES013821 Knudsen (PI) 07/01/05 – 05/31/08
Perinatal Breast Cancer Programming: fat and estrogens

NIH P30 ES014443 Ramos (PI) 06/04/07 – 03/31/11
Center for Environmental Genomics and Integrative Biology

NIH 1 RO1-DE017384-01A2 Kinane (PI) 07/09/07 – 05/31/12
Epithelial cell TLRs in disease susceptibility

NIH RO1-ES09120 Knudsen (PI) 02/01/98 – 05/31/07
NIH/NIEHS, Environmental Impact on the Embryonic mtDNA Genome

CDC RFA AA044 Kinane (PI) 07/10/05 – 07/09/07
Repository for Understanding Host-Microbe Interactions in Periodontal Pathogenesis

NIH P20-RR/DE17702 Greene (PI) 05/01/06 – 04/30/07
Proteomics based approach for early detection of fetal alcohol syndrome (mentor – S Datta, PI)